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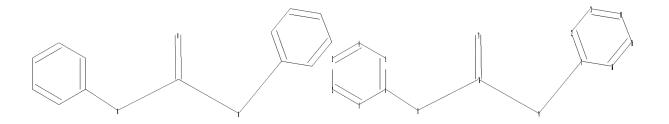
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8 9 10 11
ring nodes :
1 2 3 4 5 6 7 12 13 14 15 16
chain bonds :
6-8 7-9 8-10 9-10 10-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-12 7-16 12-13 13-14 14-15 15-16
exact/norm bonds :
6-8 7-9 8-10 9-10 10-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-12 7-16 12-13 13-14 14-15 15-16

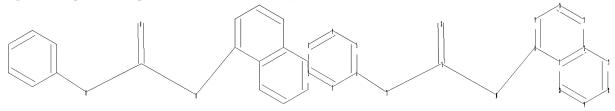
Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom

L1 STRUCTURE UPLOADED

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chain nodes :
13 14 15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 17 18 19 20
chain bonds :
6-13 8-14 13-15 14-15 15-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 7-20 8-9 9-10 10-11 11-12 12-17
17-18 18-19 19-20
exact/norm bonds :
6-13 8-14 13-15 14-15 15-16

normalized bonds:
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 7-20 8-9 9-10 10-11 11-12 12-17 17-18 18-19 19-20

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom

50 ANSWERS

L2 STRUCTURE UPLOADED

=> s 11 sss sam and 12 sss sam

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SAMPLE SEARCH INITIATED 12:11:27 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 664 TO ITERATE

100.0% PROCESSED 664 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED) SEARCH TIME: 00.00.01

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PROJECTED ITERATIONS: 11734 TO 14826 PROJECTED ANSWERS: 2266 TO 3734

L3 50 SEA SSS SAM L1 AND L2

=> s 11 and 12 sss full

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FULL SCREEN SEARCH COMPLETED - 12990 TO ITERATE

100.0% PROCESSED 12990 ITERATIONS 2738 ANSWERS

SEARCH TIME: 00.00.01

L4 2738 SEA SSS FUL L1 AND L2

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542 L4

8165 RAF

102 RAFS

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(RAF OR RAFS)

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L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:353197 CAPLUS

DOCUMENT NUMBER: 148:355817

TITLE: Preparation of heterocyclic ureas as kinase inhibitors

useful for the treatment of proliferative diseases

INVENTOR(S): Flynn, Daniel L.; Petillo, Peter A.; Kaufman, Michael

D.; Patt, William C.

PATENT ASSIGNEE(S): Deciphera Pharmaceuticals, LLC, USA

SOURCE: PCT Int. Appl., 167pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033999 WO 2008033999	A2 A3	20080320 20080807	WO 2007-US78394	20070913
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CH, CN,	CO, CR, CU	, CZ, DE, DK,	, DM, DO, DZ, EC,	EE, EG, ES, FI,
GB, GD,	SE, GH, GM	, GT, HN, HR,	HU, ID, IL, IN,	IS, JP, KE, KG,
KM, KN,	CP, KR, KZ	, LA, LC, LK,	, LR, LS, LT, LU,	LY, MA, MD, ME,
MG, MK,	IN, MW, MX	, MY, MZ, NA,	, NG, NI, NO, NZ,	OM, PG, PH, PL,
PT, RO,	RS, RU, SC	, SD, SE, SG,	, SK, SL, SM, SV,	SY, TJ, TM, TN,
TR, TT,	Z, UA, UG	, US, UZ, VC,	, VN, ZA, ZM, ZW	
RW: AT, BE,	BG, CH, CY	, CZ, DE, DK,	, EE, ES, FI, FR,	GB, GR, HU, IE,
IS, IT,	T, LU, LV	, MC, MT, NL,	, PL, PT, RO, SE,	SI, SK, TR, BF,
BJ, CF,	G, CI, CM	, GA, GN, GQ,	, GW, ML, MR, NE,	SN, TD, TG, BW,
GH, GM,	Œ, LS, MW	, MZ, NA, SD,	, SL, SZ, TZ, UG,	ZM, ZW, AM, AZ,
BY, KG,	ZZ, MD, RU	, TJ, TM, AP,	, EA, EP, OA	

US 2006-844552P P 20060914 US 2007-854293 A 20070912

OTHER SOURCE(S): MARPAT 148:355817

GΙ

$$R^3$$
 R^3
 R^3

AΒ The present invention relates to novel kinase inhibitors and modulators of general formula I (wherein X-Y is C=N or N-CH2; E1 is cyclopropyl, furyl, Ph, etc.; A is Ph, naphthyl, indanyl, etc.; Z6 is H, C1-C6alkyl, branched C3-C7alkyl, etc.; R3 and R16 are H, C1-C6 alkyl, branched C3-C7alkyl, etc.; R4 is H, C1-C6alkyl, hydroxyC1-C6alkyl, etc.; X2 is a direct bond or (un)branched C1-C6 alkyl; t is 1-3) useful for the treatment of various diseases. More particularly, the invention is concerned with such compds., kinase/compound adducts, methods of treating diseases, and methods of synthesis of the compds. Preferably, the compds. are useful for the modulation of kinase activity of Raf kinases and disease polymorphs thereof. Compds. of the present invention find utility in the treatment of mammalian cancers and especially human cancers including but not limited to malignant melanoma, colorectal cancer, ovarian cancer, papillary thyroid carcinoma, non small cell lung cancer, and mesothelioma. Compds. of the present invention also find utility in the treatment of rheumatoid arthritis and retinopathies including diabetic retinal neuropathy and macular degeneration. Example compound II was prepared by reacting 7-amino-3-(3-amino-4-fluorophenyl)-1-methyl-3,4dihydropyrimido[4,5-d]pyrimidin-2(1H)-one (preparation given) and prop-1-en-2-yl 3-tert-butyl-1-phenyl-1H-pyrazol-5-ylcarbamate (preparation given). In general, the I tested exhibited >50 % inhibition activity at $0.2-2~\mu\text{M}$ concentration in V600E B- Raf kinase and C-Raf kinase assays. In general, the I tested exhibited >50 % inhibition of proliferation at 1-10uM concentration against A375 cells. 1011463-01-6P, 1-[5-[1-Ethyl-7-(methylamino)-2-oxo-1,2dihydropyrido[4,3-d]pyrimidin-3(4H)-yl]-2-fluoro-4-methylphenyl]-3-(naphthalen-1-yl)urea 1011463-02-7P, 1-[5-[1-Ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-d]pyrimidin-3(4H)-yl]-2fluorophenyl]-3-(naphthalen-1-yl)urea 1011463-03-8P, 1-[4-Chloro-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-Chloro-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-Chloro-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-Chloro-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-Chloro-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-chloro-5-[4-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-ethyl-7-(methylamino)-2-oxo-1,2-dihydropyrido[4,3-1-[4-ethyl-7-(methylamino]-2-oxo-1,2-dihydropyrido[4,3-1-[4-ethyl-7-[d]pyrimidin-3(4H)-y1]-2-fluoropheny1]-3-(naphthalen-1-y1)urea RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(drug candidate; preparation of heterocyclic ureas as kinase inhibitors useful for treatment of proliferative diseases)

RN 1011463-01-6 CAPLUS

CN Urea, N-[5-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrido[4,3-d]pyrimidin-3(2H)-yl]-2-fluoro-4-methylphenyl]-N'-1-naphthalenyl- (CAINDEX NAME)

RN 1011463-02-7 CAPLUS

CN Urea, N-[5-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrido[4,3-d]pyrimidin-3(2H)-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1011463-03-8 CAPLUS

CN Urea, N-[4-chloro-5-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrido[4,3-d]pyrimidin-3(2H)-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:353037 CAPLUS

DOCUMENT NUMBER: 148:379650

TITLE: Preparation of heterocyclic ureas as kinase inhibitors

useful for the treatment of proliferative and

inflammatory diseases

INVENTOR(S): Flynn, Daniel L.; Kaufman, Michael D.; Patt, William

C.; Petillo, Peter A.

PATENT ASSIGNEE(S): Deciphera Pharmaceuticals, Llc., USA

SOURCE: PCT Int. Appl., 298pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.					KIND			_	APPL	ICAT	ION I	NO.						
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	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ТJ,	TM,	TN,		
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Y APPLN. INFO.:	2008034008 A2 20080320 WO 2007-US78408 2008034008 A3 20080710 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA 20080114006 A1 20080515 US 2007-854354 Y APPLN. INFO.:	2008034008 A2 20080320 WO 2007-US78408 2008034008 A3 20080710 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA 20080114006 A1 20080515 US 2007-854354 Y APPLN. INFO::	2008034008 A2 20080320 WO 2007-US78408 2 2008034008 A3 20080710 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA 20080114006 A1 20080515 US 2007-854354 2 Y APPLN. INFO::	2008034008 A2 20080320 WO 2007-US78408 20070 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA 20080114006 A1 20080515 US 2007-854354 20070 Y APPLN. INFO.:		

OTHER SOURCE(S): MARPAT 148:379650

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ΙI

AB The present invention relates to novel kinase inhibitors and modulators of general formula I (wherein E1 is cyclopropyl, furyl, Ph, etc.; A is Ph,

naphthyl, indanyl, etc.; Z6 is H, C1-C6alkyl, branched C3-C7alkyl, etc.; R3 and R16 are H, C1-C6 alkyl, branched C3-C7alkyl, etc.; R4 is H, C1-C6alkyl, hydroxyC1-C6alkyl, etc.; X2 is a direct bond or (un)branched C1-C6 alkyl; t is 1-3) useful for the treatment of various diseases. More particularly, the invention is concerned with such compds., kinase/compound adducts, methods of treating diseases, and methods of synthesis of the compds. Preferably, the compds. are useful for the modulation of kinase activity of Raf kinases and disease polymorphs thereof. Compds. of the present invention find utility in the treatment of mammalian cancers and especially human cancers including but not limited to malignant melanoma, colorectal cancer, ovarian cancer, papillary thyroid carcinoma, non small cell lung cancer, and mesothelioma. Compds. of the present invention also find utility in the treatment of rheumatoid arthritis and retinopathies including diabetic retinal neuropathy and macular degeneration. Example compound II was prepared by reacting 2-amino-6-(3-amino-4-fluorophenyl)-8-methylpyrido[2,3-d]pyrimidin-7(8H)one (preparation given) and 3-tert-butyl-1-phenyl-1H-pyrazol-5-amine (preparation

given). In general, the I tested exhibited >50 % inhibition activity at 0.2-2 μ M concentration in V600E B- Raf kinase and C-Raf kinase assays. In general, the I tested exhibited >50 % inhibition of proliferation at 1-10 μ M concentration against A375 cells.

ΙT 1012873-31-2P, 1-[5-(2-Amino-8-ethyl-7-oxo-7,8-dihydropyrido[2,3d]pyrimidin-6-yl)-2-fluorophenyl]-3-(naphthalen-1-yl)urea 1012874-63-3P, 1-[2-Fluoro-4-methyl-5-[8-methyl-2-(methylamino)-7oxo-7,8-dihydropyrido[2,3-d]pyrimidin-6-yl]phenyl]-3-(naphthalen-1-yl)urea 1012874-98-4P, 1-[5-(2-Amino-8-methyl-7-oxo-7,8-dihydropyrido[2,3d]pyrimidin-6-yl)-2-fluoro-4-methylphenyl]-3-(4-bromonaphthalen-1-yl)urea 1012874-99-5P, 1-[5-(2-Amino-8-methyl-7-oxo-7,8-dihydropyrido[2,3-methyl-7-oxo-7,8-dihydropyrido]]d]pyrimidin-6-y1)-2-fluoro-4-methylphenyl]-3-(4-chloronaphthalen-1-y1)urea 1012875-02-3P, 1-[5-[2-[[2-(Dimethylamino)ethyl]amino]-8-methyl-7oxo-7,8-dihydropyrido[2,3-d]pyrimidin-6-y1]-2-fluorophenyl]-3-(naphthalen-1-y1) urea 1012875-23-8P, 1-[5-(2-Amino-8-methyl-7-oxo-7,8-methyl-7dihydropyrido[2,3-d]pyrimidin-6-yl)-2-fluorophenyl]-3-(naphthalen-1yl)urea 1012875-98-7P, 1-[2-Fluoro-5-[8-isopropyl-2-(methylamino)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-6-yl]phenyl]-3-(naphthalen-1-yl)urea 1012877-09-6P 1012877-18-7P 1012877-21-2P 1012877-30-3P 1012877-48-3P 1012880-45-3P, 1-[5-(2-Amino-8-ethyl-7-oxo-7, 8-dihydropyrido[2,3d]pyrimidin-6-yl)-2-fluorophenyl]-3-(naphthalen-1-yl)urea hydrochloride RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(drug candidate; preparation of heterocyclic ureas as kinase inhibitors useful for the treatment of proliferative and inflammatory diseases) 1012873-31-2 CAPLUS

CN Urea, N-[5-(2-amino-8-ethyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-6-yl)-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN

RN 1012874-63-3 CAPLUS

CN Urea, N-[5-[7,8-dihydro-8-methyl-2-(methylamino)-7-oxopyrido[2,3-d]pyrimidin-6-yl]-2-fluoro-4-methylphenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012874-98-4 CAPLUS

CN Urea, N-[5-(2-amino-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-6-yl)-2-fluoro-4-methylphenyl]-N'-(4-bromo-1-naphthalenyl)- (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ \text{Me} & & & \\ & & & \\ \text{N} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 1012874-99-5 CAPLUS

CN Urea, N-[5-(2-amino-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-6-yl)-2-fluoro-4-methylphenyl]-N'-(4-chloro-1-naphthalenyl)- (CA INDEX NAME)

RN 1012875-02-3 CAPLUS

CN Urea, N-[5-[2-[[2-(dimethylamino)ethyl]amino]-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-6-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

$$\begin{array}{c} \text{Me}_2\text{N-CH}_2\text{-CH}_2\text{-NH} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{C} \\ \text{O} \\ \end{array}$$

RN 1012875-23-8 CAPLUS

CN Urea, N-[5-(2-amino-7,8-dihydro-8-methyl-7-oxopyrido[2,3-d]pyrimidin-6-yl)-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & & \\ & & \\ \text{H}_2\text{N} & \text{N} & \text{O} & \text{NH} \\ & & \\ \text{N} & & \\ & & \\ \text{F} & & \\ \end{array}$$

RN 1012875-98-7 CAPLUS

CN Urea, N-[5-[7,8-dihydro-2-(methylamino)-8-(1-methylethyl)-7-oxopyrido[2,3-d]pyrimidin-6-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012877-09-6 CAPLUS

CN Urea, N-[5-(1-ethyl-1,2-dihydro-2-oxo-1,6-naphthyridin-3-yl)-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012877-18-7 CAPLUS

CN Urea, N-[5-[1-ethyl-1,2-dihydro-7-(methylamino)-2-oxo-1,6-naphthyridin-3-yl]-2-fluoro-4-methylphenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012877-21-2 CAPLUS

CN Urea, N-[5-[1-ethyl-1,2-dihydro-7-(methylamino)-2-oxo-1,6-naphthyridin-3-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012877-30-3 CAPLUS

CN Urea, N-[4-chloro-5-[1-ethyl-1,2-dihydro-7-(methylamino)-2-oxo-1,6-naphthyridin-3-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012877-48-3 CAPLUS

CN Urea, N-[4-chloro-5-[1,2-dihydro-1-methyl-7-(methylamino)-2-oxo-1,6-naphthyridin-3-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 1012880-45-3 CAPLUS

CN Urea, N-[5-(2-amino-8-ethyl-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-6-yl)-2-fluorophenyl]-N'-1-naphthalenyl-, hydrochloride (1:1) (CA INDEX NAME)

● HCl

(preparation of heterocyclic ureas as kinase inhibitors useful for the treatment of proliferative and inflammatory diseases)

RN 1012882-99-3 CAPLUS

CN Urea, N-[5-[7,8-dihydro-8-methyl-2-(methylthio)-7-oxopyrido[2,3-d]pyrimidin-6-yl]-2-fluorophenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:381061 CAPLUS

DOCUMENT NUMBER: 144:412508

TITLE: Preparation of imidazo[4,5-b]pyridin-2-ones and

oxazolo[4,5-b]pyridin-2-ones as inhibitors of

RAF kinase

INVENTOR(S): Niculescu-Duvaz, Dan; Springer, Caroline Joy; Gill,

Adrian Liam; Taylor, Richard David; Marais, Richard Malcolm; Dijkstra, Harmen; Gaulon, Catherine; Menard,

Delphine; Roman Vela, Esteban

PATENT ASSIGNEE(S): Cancer Research Technology Limited, UK; Institute of

Cancer Research Royal Cancer Hospital; Astex

Therapeutics Limited

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIN	D	DATE			APF	LICAT		DATE					
WO	2006	A1 200604			0427		WO	2005-		20051021								
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BE	B, BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS	JP,	KE,	KG,	KM,	KP,	KR,	KZ,	
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	
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		SK,	SL,	SM,	SY,	TJ,	TM,	TN,	TR,	ΤT	, TZ,	UA,	UG,	US,	UZ,	VC,	VN,	
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		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML	MR,	ΝE,	SN,	TD,	ΤG,	BW,	GH,	
		GM,	ΚE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ	Z, TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,	
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CA	2584				A1	2006	0427		CA	2005-								
EP	1812	312433			A1 20070801					EΡ	2005-							
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			HR,	MK,	YU													
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					A 200808				BR 2005-16234									
IN 2007KN01693			A 20070			-												
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US 20070287838				A1		2007	1213			2007-		-			0070			
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OTHER SOURCE(S): MARPAT 144:412508

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$$R^1$$
 R^2
 $NR?^1$
 R^3
 R^4

AB Title compds. [I; J = O, NRn1; Rn1, Rn2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl; Y = CH, N; Q = (CH2)jM(CH2)k; j, k = 0-2; j+k = 0-2; M = O, S, NH, NMe, CH2; R1-R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, acyl; R1R2 = CH:CHCH:CH; L = linker formed by a chain of 2-4 specified linker moieties; A = aryl, heteroaryl, carbocyclyl, heterocyclyl], were prepared Thus, 4-chloro-3-trifluoromethylphenyl isothiocyanate and 7-(4-aminophenoxy)-1H-imidazo[4,5-b]pyridin-2(3H)-one were stirred together for 3 days in THF to give 1-[4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yloxy)phenyl]-3-(4-chloro-3-trifluoromethylphenyl)thiourea. In a BRAF V600E kinase inhibition assay, ≥3 I had IC50's of <0.01 μM.

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

RN 884339-11-1 CAPLUS

884339-11-1P 884339-12-2P

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)oxy]-1-naphthalenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:656575 CAPLUS

DOCUMENT NUMBER: 139:197476

TITLE: Preparation of aryl heterocyclyl ureas with

raf kinase and angiogenesis inhibiting

activity

INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James;

Hatoum-Makdad, Holia

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIND DATE				APPL	ICAT	DATE							
WO	2003068223				A1 20030821				WO 2	003-		20030211						
	₩:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
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		UG,	US,	UΖ,	VN,	YU,	ZA,	ZM,	ZW									
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		KG,	KZ,	MD,	RU,	ΤJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
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		вJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
AU	AU 2003210969					·	2003	0904		AU 2	003-	·	20030211					
US 20040023961					A1	20040205 US 2003-361						3618	44		2	20030211		
PRIORIT	Y APP	LN.	INFO	.:						US 2	002-]	P 20020211					
									,	WO 2	003-	1	W 20030211					

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AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl) pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy) naphthylamine (prepns. given) and CDI in CH2Cl2 afforded 80% I which showed IC50 of < 1 μ M in in vitro raf kinase and in vitro Flk-1 ELISA assay.

Ι

294849-72-2P 294849-74-4P 294849-76-6P 294849-78-8P 294849-80-2P 294849-82-4P 294849-84-6P 294849-86-8P 294849-88-0P 294849-92-6P 294849-94-8P 294849-97-1P 294850-00-3P 294850-02-5P 294850-04-7P 294850-06-9P 294850-09-2P 294850-12-7P 294850-15-0P 294850-18-3P 294850-21-8P 294850-24-1P 294850-27-4P 294850-29-6P 294850-31-0P 294850-33-2P 294850-35-4P 294850-37-6P 294850-39-8P 294850-41-2P 294850-43-4P 294850-45-6P 294850-47-8P 294850-49-0P 294850-51-4P 294850-53-6P 294850-55-8P 294850-57-0P 294850-59-2P 294850-61-6P 294850-63-8P 294850-65-0P 294850-67-2P 294850-69-4P 294850-71-8P 294850-73-0P 294850-76-3P 294850-79-6P 294850-81-0P 294850-84-3P 294850-87-6P 294850-90-1P 294850-93-4P 294850-96-7P 294851-02-8P 294851-05-1P 294851-07-3P 294851-09-5P 294851-11-9P 294851-14-2P 294851-18-6P 294851-20-0P 294851-22-2P 294851-24-4P 294851-26-6P 294851-28-8P 294851-32-4P 294851-34-6P 294851-36-8P 294851-38-0P 294851-40-4P 294851-42-6P 294851-44-8P 294851-46-0P 294851-48-2P 294851-50-6P 294851-52-8P 294851-56-2P 294851-58-4P 294851-60-8P 294851-62-0P 294851-64-2P 294851-66-4P 294851-68-6P 294851-70-0P 294851-72-2P 294851-76-6P 294855-56-4P 340825-40-3P 340825-41-4P 340825-46-9P 340825-47-0P 340825-48-1P 340825-49-2P 340825-51-6P 340825-52-7P 340825-53-8P 340825-54-9P 340825-55-0P 340825-56-1P 501365-69-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

RN 294849-72-2 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

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RN 294849-74-4 CAPLUS

CN Urea, N-(4-methyl[1,1'-biphenyl]-3-yl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-76-6 CAPLUS

CN Urea, N-[4-(1,1-dimethylethyl)[1,1'-biphenyl]-2-yl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-78-8 CAPLUS

CN Urea, N-[2-methyl-5-(1-methylethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-80-2 CAPLUS

CN Urea, N-[2-methoxy-5-(1-methylpropyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-82-4 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-(methoxymethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-84-6 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-86-8 CAPLUS

CN

Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

<u>.</u>

Me

RN 294849-88-0 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-92-6 CAPLUS

CN Urea, N-[5-(1,1-dimethylpropyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

MeO.

RN 294849-94-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(1H-pyrazol-4-yl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294849-97-1 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(2-methyl-5-pyrimidinyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-00-3 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(3-hydroxypropyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

294850-02-5 CAPLUS RN

Urea, N-[5-(1,1-dimethylethyl)-2-(4-morpholinylcarbonyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)CN

294850-04-7 CAPLUS

RN

t-Bu

CN Acetamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 294850-06-9 CAPLUS

CN Urea, N-(3-methyl-2-naphthalenyl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

294850-09-2 CAPLUS Urea, N-[3-(2,3-dihydroxypropyl)-5-(1,1-dimethylethyl)-2-hydroxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME) CN

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RN 294850-12-7 CAPLUS

CN Urea, N-(2,3-dimethyl-1H-indol-5-yl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-15-0 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methyl-3-[3-[(tetrahydro-2H-pyran-2-yl)oxy]-1-propyn-1-yl]phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} \\ \hline & \text{O}-\text{CH}_2-\text{C} \end{array} \\ \hline \\ & \text{Bu-t}$$

RN 294850-18-3 CAPLUS
CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-21-8 CAPLUS

CN Urea, N-[5-(2,2-dimethyl-1-oxopropyl)-2-methylphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-24-1 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-(3-hydroxy-1-propyn-1-yl)-2-methylphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \\ \text{HO-CH}_2\text{-C} \\ \end{array} \\ \text{Bu-t} \\ \\ \end{array}$$

RN 294850-27-4 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(3-hydroxy-1-propyn-1-yl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-29-6 CAPLUS

CN Urea, N-[3-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-31-0 CAPLUS

CN Urea, N-[3-(2,3-dihydroxypropyl)-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-33-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethoxy)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-35-4 CAPLUS

CN Urea, N-[5-(1-cyanocyclopropyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-37-6 CAPLUS

CN Urea, N-[3-[2-(diethylamino)ethyl]-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \\ \text{Et}_2\text{N}-\text{CH}_2-\text{CH}_2 \\ \end{array} \\ \text{Bu-t}$$

RN 294850-39-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(1,3-dioxolan-2-yl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-41-2 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-(1-pyrrolidinyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-43-4 CAPLUS

CN Urea, N-[2-(dimethylamino)-5-(1,1-dimethylethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-45-6 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-propoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-47-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(hydroxymethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-49-0 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(2,6-dimethyl-4-morpholinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

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RN 294850-51-4 CAPLUS

CN Urea, N-(5-cyclohexyl-2-methoxyphenyl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

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RN 294850-53-6 CAPLUS

CN Urea, N-[2,4-dimethoxy-5-(trifluoromethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-55-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxy-3-nitrophenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-57-0 CAPLUS

Urea, N-[3-amino-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(6-methyl-3-pyridinyl)-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-59-2 CAPLUS

CN Acetamide, N-acetyl-N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

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RN 294850-61-6 CAPLUS

CN Urea, N-[6-(1,1-dimethylethyl)-3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzoxazin-8-yl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-63-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-ethoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-65-0 CAPLUS

Urea, N-[5-(1,1-dimethylethyl)-2-(1-methylethoxy)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-67-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(1H-imidazol-1-yl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-69-4 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-(ethylamino)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-71-8 CAPLUS

CN Methanesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-N-(methylsulfonyl)- (CA INDEX NAME)

RN 294850-73-0 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(1-methyl-1H-pyrazol-4-yl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-76-3 CAPLUS

CN Urea, N-[2-(methylsulfinyl)-5-(trifluoromethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294850-79-6 CAPLUS

CN Urea, N-[4-[6-[[bis(2-methoxyethyl)amino]methyl]-3-pyridinyl]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxyphenyl]- (CA INDEX NAME)

RN 294850-81-0 CAPLUS
CN Acetamide, N-[1-[[5-[4-[[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]-1-naphthalenyl]-2-pyridinyl]methyl]-3-pyrrolidinyl]- (CA INDEX NAME)

RN 294850-84-3 CAPLUS
CN Urea, N-(1-acetyl-2,3-dihydro-3,3-dimethyl-1H-indol-5-yl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

294850-87-6 CAPLUS Propanamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl CN]- (CA INDEX NAME)

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RN 294850-90-1 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methyl-7-benzoxazolyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

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RN 294850-93-4 CAPLUS

CN

Urea, N-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]-N'-[3-[(trifluoromethyl)sulfonyl]phenyl]- (CA INDEX NAME)

RN 294850-96-7 CAPLUS

CN Propanamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-2-methyl- (CA INDEX NAME)

RN 294851-02-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2,3-dihydro-2-oxo-7-benzoxazolyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

t-Bu

RN

CN

294851-05-1 CAPLUS
Urea, N-[3-cyano-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-07-3 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-7-benzoxazolyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-09-5 CAPLUS

CN Benzenesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 294851-11-9 CAPLUS

CN Ethanesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 294851-14-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(methylthio)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-18-6 CAPLUS

CN Ethanesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-2,2,2-trifluoro- (CA INDEX NAME)

RN 294851-20-0 CAPLUS

CN Methanesulfonamide, N-[5-[4-[[[[5-(1,1-dimethylethyl)-2-methylphenyl]amino]carbonyl]amino]-1-naphthalenyl]-2-pyrazinyl]- (CA INDEX NAME)

||

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RN 294851-22-2 CAPLUS

CN Urea, N-[4-[6-[[bis(2-cyanoethyl)amino]methyl]-3-pyridinyl]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxyphenyl]- (CA INDEX NAME)

RN

CN

294851-24-4 CAPLUS
Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(4-methyl-1-piperazinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-26-6 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-thiomorpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-28-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(2,6-dimethyl-1-piperidinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-32-4 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(tetrahydro-2H-pyran-4-yl)amino]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

294851-34-6 CAPLUS RN

Urea, N-[4-[6-[[(2-cyanoethyl)[(tetrahydro-2-furanyl)methyl]amino]methyl]-3-pyridinyl]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-(CA INDEX NAME) CN

RN 294851-36-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[[2-(methoxymethyl)-4-morpholinyl]methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-38-0 CAPLUS

Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(2-methyl-3-oxo-1-piperazinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-40-4 CAPLUS

CN 3-Piperidinecarboxamide, 1-[[5-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]-1-naphthalenyl]-2-pyridinyl]methyl]-(CA INDEX NAME)

RN 294851-42-6 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(1-oxido-4-thiomorpholinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-44-8 CAPLUS

CN Urea, N-(2,3-dihydro-3,3-dimethyl-2-oxo-1H-indol-5-yl)-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN

294851-46-0 CAPLUS Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[(3-oxo-1-piperazinyl)methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME) CN

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RN 294851-48-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[[(tetrahydro-3-furanyl)amino]methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

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RN 294851-50-6 CAPLUS

CN Urea, N-[4-[6-[[(2-cyanoethyl)(3-pyridinylmethyl)amino]methyl]-3-pyridinyl]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-(CA INDEX NAME)

RN 294851-52-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(2-oxa-5-azabicyclo[2.2.1]hept-5-ylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-56-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-[[4-(3-methoxyphenyl)-1-piperazinyl]methyl]-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-58-4 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylcarbonyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-60-8 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[5-(4-morpholinylmethyl)-2-pyrazinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-62-0 CAPLUS

CN Urea, N-[6-(1,1-dimethylethyl)-3,4-dihydro-3-oxo-2H-1,4-benzoxazin-8-yl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

294851-64-2 CAPLUS Urea, N-[3-amino-5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME) CN

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RN 294851-66-4 CAPLUS

CN Acetamide, N-[5-[4-[[[5-(1,1-dimethylethyl)-2-methoxyphenyl]amino]carbonyl]amino]-1-naphthalenyl]-2-pyridinyl]- (CA INDEX NAME)

RN 294851-68-6 CAPLUS

CN Acetamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-N-methyl- (CA INDEX NAME)

Me

RN 294851-70-0 CAPLUS
CN Acetamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-2,2,2-trifluoro- (CA INDEX NAME)

RN 294851-72-2 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[6-(3-pyridinyloxy)-3-pyridinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 294851-76-6 CAPLUS

CN Methanesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 294855-56-4 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[2-(4-morpholinylmethyl)-5-pyrimidinyl]-1-naphthalenyl]- (CA INDEX NAME)

RN 340825-40-3 CAPLUS

CN Urea, N-[4-[(2-amino-4-pyridinyl)oxy]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methylphenyl]- (CA INDEX NAME)

RN

 $340825-41-4 \quad CAPLUS \\ Urea, \quad N-[5-(1,1-dimethylethyl)-2-(4-morpholinyl)phenyl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- \quad (CA INDEX NAME)$ CN

PAGE 1-A



RN 340825-46-9 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[(2-methoxy-4-pyridinyl)oxy]-1-naphthalenyl]- (CA INDEX NAME)

RN 340825-47-0 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-[(2-methyl-4-pyridinyl)oxy]-1-naphthalenyl]- (CA INDEX NAME)

RN 340825-48-1 CAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2,3-dimethoxyphenyl]-N'-[4-[(2-methoxy-4-pyridinyl)oxy]-1-naphthalenyl]- (CA INDEX NAME)

RN 340825-49-2 CAPLUS

CN Benzamide, 5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-(4-pyridinyloxy)-1-naphthalenyl]amino]carbonyl]amino]- (CA INDEX NAME)

RN 340825-51-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-(4-pyridinyloxy)-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 340825-52-7 CAPLUS

CN Acetamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-(4-pyridinyloxy)-1-naphthalenyl]amino]carbonyl]amino]phenyl]- (CA INDEX NAME)

RN 340825-53-8 CAPLUS

CN Urea, N'-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[[4-(4-pyridinyloxy)-1-naphthalenyl]amino]carbonyl]amino]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 340825-54-9 CAPLUS

CN Urea, N-[4-[(2-amino-4-pyridinyl)oxy]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2,3-dimethoxyphenyl]- (CA INDEX NAME)

RN 340825-55-0 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2,3-dimethoxyphenyl]-N'-[4-[[2-(methylamino)-4-pyridinyl]oxy]-1-naphthalenyl]- (CA INDEX NAME)

RN 340825-56-1 CAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2,3-dimethoxyphenyl]-N'-[4-[[2-[(1-phenylethyl)amino]-4-pyridinyl]oxy]-1-naphthalenyl]- (CA INDEX NAME)

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RN 501365-69-1 CAPLUS
CN Acetamide, 2-[4-(1,1-dimethylethyl)-2-[[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenoxy]- (CA INDEX NAME)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:421642 CAPLUS

DOCUMENT NUMBER: 131:58658

TITLE: Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas

Miller, Scott; Osterhout, Martin; Dumas, Jacques; INVENTOR(S):

Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.;

Gunn, David; Rodriguez, Mareli; Wang, Ming

Bayer Corporation, USA PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932436	A1	19990701	WO 1998-US26081	19981222

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OTHER SOURCE(S): MARPAT 131:58658

The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepared For instance, reaction of tolyl isocyanate with 2-methoxy-5- (trifluoromethanesulfonyl)aniline in EtOAc gave title compound II. In an in

vitro raf kinase assay, all compds. displayed IC50 values between 1 nM and 10 μM_{\star}

IT 228399-62-0P 228400-96-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

RN 228399-62-0 CAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-1-naphthalenyl- (CA INDEX NAME)

RN 228400-96-2 CAPLUS

CN Urea, N-(3-methoxy-2-naphthalenyl)-N'-1-naphthalenyl- (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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